northwest US according to Dr. Whitehouse. There are no illustrations of the chest x-rays or HRCT studies in the article to aid understanding.

What conclusions can be drawn from this study regarding the image data other than there were some pleural and interstitial "changes"? It would have been very useful if the listed physiological changes could have been better correlated with the imaging findings. We don't know if the findings were unilateral or bilateral, calcified or non-calcified, thick or thin. We have no quantification whatsoever of the pleural changes which are the crux of the paper. How can one compare the imaging data in this paper to other papers? What conclusions can be reached? What extent of pleural disease is associated with the progressive physiological changes described in the paper? If there is no correlation, it should be detailed and proven.

Dr. Whitehouse repeatedly finds fault with the B-reader system and the ILO Classification process and has so for some time. I am unaware of any alternative system or meaningful proposal advanced by Dr. Whitehouse to interpret and classify or grade or list the radiographic features of chest x-rays let alone any cross-sectional (CT, HRCT) imaging study. The imaging evaluation methodology described in his paper is primitive, incomplete, and essentially useless.

Clarification of Terms

Dr. Whitehouse states the following: "Sometimes the term "asbestosis" is used as an umbrella term, covering asbestos interstitial disease and asbestos pleural disease since they are essentially the same disease process." (p 5-6)

Dr Whitehouse's statement is directly contradictory to the ATS'04 Statement definition of "asbestosis": "Asbestosis specifically refers to interstitial fibrosis caused by the deposition of asbestos fibers in the lung. It does not refer to visceral pleural fibrosis, the subpleural extensions of fibrosis into the interlobular septae or lesions of the membranous bronchioles." (p 697)

Furthermore, Dr. Whitehouse attempts to support his definition of the term" asbestosis" with a textbook quote and reference from Rosenstock: "Some investigators have used the term asbestosis to encompass nonmalignant asbestos-related pleural abnormalities" (p 6). The textbook quote in its entirety, reads as follows: "Although, some investigators have used the term asbestosis to encompass nonmalignant asbestos-related pleural abnormalities, it is employed here to refer solely to the interstitial fibrosis and accompanying peribronchiolar fibrosis found in the parenchyma of affected individuals"(11). I am appalled by this distortion of the medical literature. The Rosenstock statement is in accord with the definition of the term "asbestosis" in the ATS'04 Statement.

Dr. Whitehouse's use of the term "asbestosis" is quite clearly at odds with the ATS'04 Statement guidelines and a distortion of his own reference material. Not surprisingly, his application and use of this term has the potential to create confusion and inappropriate

conclusions. Throughout the "Updated Whitehouse Report", there are several instances where the results or outcomes from other papers and texts are compared or paralleled to Libby data. Caution must be used to avoid comparisons to sources describing data attributed to asbestosis (interstitial fibrosis) by the ATS'04 Statement definition as compared to Libby data based on the Whitehouse use of the term "asbestosis" that is all inclusive of lung parenchymal and pleural disease.

Diffuse Pleural Thickening

Dr. Whitehouse states the following: "No pulmonologist would use blunting to determine a diagnosis of asbestos pleural disease (p57)....ATS (2004) does not include blunting in the diagnostic criteria for asbestos related disease (p58)...The 3mm requirement is contrary to standard practice in diagnosing asbestos pleural disease(p60)..."

As I review the numerous paragraphs of the "Updated Whitehouse Report", two key issues seem to be the threshold of pleural thickness at 3mm for pleural plaques and the involvement (blunting or obliteration) of the costophrenic angle as it relates to diffuse pleural thickening (DPT).

Dr. Whitehouse states the following: "Diffuse pleural fibrosis extends continuously over a portion of the visceral pleura, often causing adhesions to the parietal pleura." (p12-13)

The entire quotation from the ATS'04 Statement is as follows: "Diffuse pleural fibrosis extends continuously over a portion of the visceral pleura, often causing adhesions to the parietal pleura, involving the fissures and obliterating the costophrenic angle. The newly revised ILO classification (2000) recognizes pleural thickening as diffuse 'only in the presence of and in continuity with, an obliterated costophrenic angle'" (p 707). This quote would appear to contradict Dr. Whitehouse's comment above regarding blunting of the costophrenic angle. The surgically excised and selective literature quotations continue.

Sargent authored several papers but two relevant to this discussion were published in 1978 and 1984 (12-13). The earlier paper describes pleural thickening and calls attention to it as a marker of asbestos pleural disease, attributing its development to previous asbestos pleural effusion. The latter paper describes subpleural fat and distinguishes it from pleural thickening and reviews 30 patients with chest CT. In these two papers, the concept of diffuse pleural thickening associated with obliteration of the costophrenic angle is developed. Based upon his observations, he concluded that DPT obliterated the costophrenic angle while subpleural fat and pleural plaques did not. Sargent participated in the development of the 1980 ILO Guidelines. He was a member of the ACR Pneumoconiosis Task Force and a faculty member for the ACR course on pneumoconioses for many years and popularized the concept.

McLoud in 1985 discussed DPT observed in a group of asbestos exposed workers and determined that the costophrenic angle may or may not be involved (14). She further extended Sargent's definition of DPT with the requirement of extending over at least one

fourth of the chest wall. Using these parameters, McLoud lists 185 workers as having DPT. Fifty-eight or 31% of the total had DPT attributed to previous asbestos pleural effusion and 90% of this group had obliteration of the costophrenic angle similar to Sargent's experience. A second group of 47 workers or 25% classified as DPT did not have involvement of the costophrenic angle and the pleural thickening was attributed to multiple confluent pleural plaques. Viewing oblique chest radiographs that more clearly characterized the confluent pleural plaques made this distinction. While the confluent plaques appeared smooth on the frontal view, they appeared more irregular on the oblique views. The remaining 80 workers classified as DPT had pleural thickening due to malignancy, infection, trauma, subpleural fat, asbestosis, and unknown. According to McLoud, those classified as DPT but without costophrenic angle involvement (confluent pleural plaques) had no physiologic abnormalities on pulmonary function studies while those with costophrenic angle obliteration did have significant physiologic deficits. The definition in the Fraser and Pare text mentioned in the "Updated Report" is simply a reference to McLoud's article discussed above.

Sargent in '78 was apparently calling attention at that time to the presence of non-calcified pleural thickening as indicative of asbestos exposure in addition to the more commonly and easily recognized calcified pleural plaque. He distinguished between pleural thickening due to confluent plaques of the parietal pleura that did not involve the costophrenic angle and pleural thickening following asbestos effusion and involving the visceral pleura that did involve the costophrenic angle. Both Sargent and McLoud mention the non-specific nature of pleural thickening with involvement of the costophrenic angle since this constellation of findings is seen in other non-asbestos related processes as listed by McLoud. Care was also taken to describe the thickening as smooth to avoid confusion with mesothelioma.

Dr. Whitehouse states the following: "No blunting requirement appeared in the earlier version of the ILO guidelines." (p 57)

That is not an accurate statement. The 1980 ILO Guidelines described pleural thickening as diffuse involving the visceral pleura and circumscribed (non-calcified hyaline plaques) as involvement of the parietal pleura (15). The word 'diffuse' is stated to refer to the tendency to produce a general veiling of the lung parenchymal detail however in some cases the shadow produces a sharply defined line along the chest wall due to it being seen in profile. Note 13 of the 1980 ILO Guidelines states "Diffuse thickening is less specific to past dust exposure and accompanies costophrenic angle obliteration." The 1980 Guidelines are organized with a narrative of "Complete Classification" supported elsewhere by "Explanatory Notes," a somewhat unsettling arrangement. The "Notes" were intended to reduce ambiguities and to bring forth experience from previous "Classifications." The 2000 ILO Guidelines are presented in a more continuous, readable form consolidating the notes from the previous edition into the main body of text entitled " Specific instructions for use of the Complete Classification" (16). This reorganization promotes an easier understanding of the various components without having to refer back and forth from one page to the other. The 2000 Guidelines discuss DPT as historically referring to thickening of the visceral pleura. The Guidelines further state that " diffuse

pleural thickening extending up the lateral chest wall is recorded only in the presence of, and in continuity with, an obliterated costophrenic angle." This is basically a restatement of the 1980 Guidelines with some clarity added by consolidating the notes and text. The 2000 Guidelines are consistent with both Sargent's and McLoud's papers: visceral pleural thickening is associated with costophrenic angle obliteration; parietal pleural thickening as plaques and confluent plaques generally do not involve the costophrenic angle. The goal is to distinguish these two different types of pleural involvement since they have differing physiologic consequences (McLoud). But in medicine there is no "never" or " always". It is not always possible to distinguish between the two different types of pleural involvement by conventional radiography. Also, a blunted costophrenic angle can occur in the absence of diffuse pleural thickening such as in the case of a pleural effusion. Recent textbooks as well as the 2004 ATS Statement mention obliteration of the costophrenic angle in association with diffuse pleural thickening (17). A recent paper also underscores the importance of the obliteration of the costophrenic angle in DPT (18).

Dr. Whitehouse states the following: "There is no scientific basis for a requirement of 3mm thickness in its scoring definition of 'diffuse pleural thickening'"(p59)

The threshold of "about 3mm" from the 2000 ILO Guidelines for the detection of pleural plaques and pleural thickening is obviously an issue for Dr. Whitehouse. Over the last 30 years or so, many observations have been recorded measuring the "normal" pleural stripe on conventional radiographs. The measurements have varied with posterior anterior (PA) views of the chest and oblique views and varied in different areas of the thorax. Over this time period the film techniques changed with wider latitude film being more commonly employed which provided a broader scale of contrast with grayer films as compared to the older black and white films with a shorter scale of contrast. These changes in film technique brought a different perspective and clarity to what was "normal." The inner chest walls and pleural surfaces were more clearly visualized.

One of the contributing and clarifying factors to the 3mm threshold was Sargent's 1984 paper on subpleural fat in asbestos exposed workers. It reported that 48% of workers' chest radiographs interpreted as indicating pleural thickening were in fact due to deposition of subpleural fat when evaluated by chest CT. Furthermore the subpleural fat depositions were not dependent on body habitus although could be increased in overweight individuals. As chest CT became more widespread through the 80's and through today, the recognition of subpleural fat has became commonplace. Thus the improvements in conventional chest x-ray technology combined with the recognition of normal subpleural fat and its potential confusion with pleural abnormalities promoted a need for clarification. In a personal communication from a member of the discussion group that formulated the 2000 ILO Guidelines, the group wanted to take into consideration the issue of subpleural fat and the contributions developed by chest CT since the previous guidelines in 1980. Thus the 3mm threshold was adopted.

The adoption of a 3mm imaging threshold for diffuse pleural thickening is not unique to the 2000 ILO Guidelines. Fraser and Pare, a reference quoted by Dr. Whitehouse, describes diffuse pleural thickening on CT as "a continuous area of pleural thickening greater than 3mm extends for more than 8 cm craniocaudally and 5 cm around the perimeter of the hemithorax."(19). Im et al provide a very detailed discussion of the pleura on HRCT (20). They stress the importance of window level and width, slice thickness, angle of the imaging plane to the various ribs, and the importance of a familiarity with pleural and subpleural anatomy in the diagnosis of pleural thickening. They also point out the pitfalls to be avoided due to such things as intercostal veins, as well as transverse thoracic and subcostal muscles.

Dr. Whitehouse states that the 2004 ATS Official Statement stipulates a 1mm threshold for diffuse pleural thickening on p 707. This description of pleural thickening in the ATS'04 Statement relates to pathologic specimens not chest radiographs or chest CT's. HRCT can detect pleural thickening at perhaps the 1-2mm thickness level (21).

References:

1. Crapo J. Written statement/testimony before United States Senate Committee on the Judiciary: A fair and efficient system to resolve claims of victims for bodily injury caused by asbestos, and for other purposes. April 26. 2005. http://judiciary.senate.gov/print_testimony.cfm?id=1482&wit_id=4237

2. American Thoracic Society. Diagnosis and initial management of nonmalignant diseases related to asbestos. Am J Respir Crit Care Med 2004; 170:691-715.

3. Attfield M, Petsonk E. Advanced pneumoconiosis among working underground coal miners-eastern Kentucky and southwestern Virginia, 2006. MMWR,2007; 56(26):652-655

4. Antao V, Petsonk E, Attfield M. Advanced cases of coal workers pneumoconiosis-two counties Virginia, 2006. MMWR 2006; 55(33): 909-913.

5. Lockey et al. Pulmonary changes after exposure to vermiculite contaminated with fibrous tremolite. *American Review of Respiratory Disease* 1984; 129: 952-958.

6. McDonald J, Sebastien P, Armstrong B. Radiologic survey of past and present vermiculite miners exposed to tremolite. *British Journal of Industrial Medicine* 1986; 43:445-449.

7. Amandus H et al, The morbidity and mortality of vermiculite miners and millers exposed to actinolite-tremolite: Part III. Radiographic findings *American Journal of Industrial Medicine* 1987;11:27-37.

8. Piepins et al. Radiographic abnormalities and exposure to asbestos contaminated vermiculite in the community of Libby, Montana USA. *Environmental Health Perspectives*, 2003; 111(14): 1753-1759.

9. Rohs A et al. Low-level fiber induced radiographic changes caused by Libby vermiculite. A 25-year follow-up study. *American Journal of Respiratory and Critical Care Medicine* 2008; 177:630-637.

10. Whitehouse A. Asbestos-related pleural disease due to tremolite associated with progressive loss of lung function: serial observations in 123 miners, family members, and residents of Libby, Montana. *American Journal of Industrial Medicine* 2004; 46:219-225.

11. Brodkin C, Rosenstock L, Asbestosis and asbestos related pleural disease, In Rosenstock L, Cullen M, Brodkin C, Redlich C. Textbook of Clinical Occupational and Environmental Medicine 2nd Ed. Saunders, Elsevier Health Sciences, Philadelphia. 2004; p 374.

12. Sargent E, et al. Bilateral pleural thickening: a manifestation of asbestos dust exposure. Am Journ Roentgenology 1978; 131:579-585.

13. Sargent E, et al. Subpleural fat pads in patients exposed to asbestos: distinction from non-calcified pleural plaques. Radiology 1984;152:273-277.

14. McLoud T, et al. Diffuse pleural thickening in an asbestos- exposed population: prevalence and causes. Am Journ Roentgenology 1985; 144:9-18.

15. International Labour Office Geneva. Guidelines for the use of ILO International Classification of Radiographs of Pneumoconioses Rev. Ed. 1980

16. International Labour Office Geneva. Guidelines for the use of the ILO International Classification of Radiographs of Pneumoconioses Rev. Ed. 2000.

17. Hansel D, Armstrong P, Lynch D, Page McAdams H. *Imaging of Diseases of the Chest.* 4th Ed. Elsevier Mosby, Philadelphia; 2005: 450-461;1056-1062.

18. Amielle et al. Asbestos-related pleural diseases: Dimensional criteria are not appropriate to differentiate diffuse pleural thickening from pleural plaques. Am Journ Of Ind Med 2004; 45: 289-296.

19. Fraser R, Müller N, Colman N, Paré P. *Fraser and Paré's Diagnosis of Diseases of the Chest.* 4th Ed. WB Saunders, Philadelphia, 1999; Vol IV: 2430-2437.

20. Im et al. Costal pleura: appearances on high resolution CT. Radiology 1989; 171:125-131.

21. Webb W, Müller N, Naidich D. *High Resolution CT of the Lung*. 3rd Ed. Lippincott Williams & Wilkins, Philadelphia, 2001: 236-251.

Daniel A. Henry, M.D., F.A.C.R.

April 6, 2009